

IN THE SPECIFICATION

Please amend the specification as indicated below (references are to the paragraph numbers in the published application).

Please amend paragraph [0005] as indicated below:

[0005] When the solvent is toxic it may be toxic in certain applications but not in others. For example, ethanol, which maybe used as a solvent, is generally considered “bio-compatible,” however, this is clearly not the case when the target site is within the myocardium. This selective toxicity is problematic at least to the extent that a medical device carrying a therapeutic could not be universally employed but would, rather, only be usable for target ~~eites~~ sites that were not injured by the solvent.

Please amend paragraph [0007] as indicated below:

[0007] Method and apparatus to modify a fluid by passing a compound through a selectively permeable membrane ~~is~~ are provided. In one embodiment a fluid moving through a vessel is modified prior to its ejection from the vessel. This may be accomplished by urging the fluid into a mixing chamber wherein the mixing chamber is in fluid communication with an exit orifice and a passageway. This passageway may be in communication with a second chamber through a selectively permeable membrane. The fluid may then be altered by passing a compound between the mixing chamber and the second chamber through the passageway and the selectively permeable membrane.

Please amend paragraph [0020] as indicated below:

[0020] The pushing force arrow 12 demonstrates the direction of a force that may be generated at the proximal end of the catheter and used to urge the therapeutic through the inner lumen 16. Similarly, a vacuum ~~forced~~ force arrow 11 is also ~~illustrated. This one to show~~ illustrated, to show the direction of a vacuum force that may be generated at the proximal end of the catheter and used to draw compounds through the selectively permeable membrane 15 of the mixing chamber 18. In this embodiment the passing of the solvent through the selectively permeable membrane 15 is accelerated by the vacuum force 11 resident in the outer lumen 17.

Please amend paragraph [0022] as indicated below:

[0022] In use the catheter 100 would be inserted into the target site 110 to ~~deliver~~ therapeutic ~~deliver a therapeutic~~ resident within the inner lumen 16. After the catheter 100 has been inserted into the target site 110 the therapeutic containing the solvent may be pushed down the inner lumen 16 through various means including a syringe, a mechanical pump and a squeezable bladder. These means may be used not only to push the therapeutic through the lumen but also to store it prior to the catheter being used and to control the volume and rate of injection of the therapeutic.

Please amend paragraph **[0028]** as indicated below:

[0028] The selectively permeable membrane may be made from any appropriate material. The membrane may be chosen predicated upon the specific application of the catheter, upon the specific therapeutic passing through the mixing chamber or upon any combination of fluids and applications that may be encountered. A polycarbonate membrane is an example of a selectively permeable membrane 15 that may be used in certain applications. Other plausible examples are glass microfibers, PTFE (TeflonTM), polyethersulfone, nylon, polypropylene, cellulose including ~~those that~~ having ~~enzymes-linked~~ enzyme-linked surfaces, antibodies, chelating agents, absorbent coatings, and functional modifications of these materials.

Please amend paragraph **[0042]** as indicated below:

[0042] In so doing, the fluid that leaves the distal end of the needle 60 contains a higher ~~portion~~ proportion of therapeutic 64 and hardening agent 66 and a lower proportion of solvent 65 than originally combined in the first part of the mixing chamber 61. By mixing these compounds together in this fashion, the *in situ* formation of controlled release plugs can be completed. These release plugs may be beneficial to retaining therapeutic within an actively contracting and expanding target site of the body.

Please amend paragraph **[0045]** as indicated below:

[0045] The outer lumen 69 in this embodiment may be made from any suitably rigid material including surgical stainless steel, nitinol, and rigid plastics. Similarly, the internal lumens may also be made from any suitably rigid material capable of carrying fluids that preferably will also be compatible with the therapeutics or other fluids traveling through them. The therapeutics traveling through the inner lumen in this embodiment as well as in the other embodiments may include, for example, pharmaceutically active compounds, proteins, cells, oligonucleotides, ribozymes, anti-sense oligonucleotides, DNA compacting agents, gene/vector systems (i.e., any vehicle that allows for the uptake and expression of nucleic acids), nucleic

acids (including, for example, recombinant nucleic acids; naked DNA, cDNA, RNA; genomic DNA, cDNA or RNA in a non-infectious vector or in a viral vector and which further may have attached peptide targeting sequences; antisense nucleic acid (RNA or DNA); and DNA chimeras which include gene sequences and encoding for ferry proteins such as membrane translocating sequences ("MTS") and herpes simplex virus-1 ("VP22")), and viral, liposomes and cationic and anionic polymers and neutral polymers that are selected from a number of types depending on the desired application. Non-limiting examples of virus vectors or vectors derived from viral sources include adenoviral vectors, herpes simplex vectors, papilloma vectors, adeno-associated vectors, retroviral vectors, and the like. Non-limiting examples of biologically active solutes include anti-thrombogenic agents such as heparin, heparin derivatives, urokinase, and PPACK (dextrophenylalanine proline arginine chloromethylketone); antioxidants such as probucol and retinoic acid; angiogenic and anti-angiogenic agents and factors; agents blocking smooth muscle cell proliferation such as rapamycin, angiopeptin, and monoclonal antibodies capable of blocking smooth muscle cell proliferation; anti-inflammatory agents such as dexamethasone, prednisolone, corticosterone, budesonide, estrogen, sulfasalazine, acetyl salicylic acid, and mesalamine; calcium entry blockers such as verapamil, diltiazem and nifedipine; antineoplastic / antiproliferative / anti-mitotic agents such as paclitaxel, 5-fluorouracil, methotrexate, doxorubicin, daunorubicin, cyclosporine, cisplatin, vinblastine, vincristine, epothilones, endostatin, angiostatin and thymidine kinase inhibitors; antimicrobials such as triclosan, cephalosporins, aminoglycosides, and ~~niterfurantoin~~; nitrofurantoin anesthetic agents such as lidocaine, bupivacaine, and ropivacaine; nitric oxide (NO) donors such as ~~linsidomine~~, linsidomine, molsidomine, ~~L-arginine~~ L-arginine, NO-protein adducts, NO-carbohydrate adducts, polymeric or oligomeric NO adducts; anti-coagulants such as D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, antithrombin compounds, platelet receptor antagonists, anti-thrombin antibodies, anti-platelet receptor antibodies, enoxaparin, hirudin, Warafin sodium, Dicumarol, aspirin, prostaglandin inhibitors, platelet inhibitors and tick antiplatelet factors; vascular cell growth promoters such as growth factors, growth factor receptor antagonists, transcriptional activators, and translational promoters; vascular cell growth inhibitors such as growth factor inhibitors, growth factor receptor antagonists, transcriptional repressors, translational repressors, replication inhibitors, inhibitory antibodies, antibodies directed against growth factors, bifunctional molecules consisting of a growth factor and a cytotoxin, bifunctional molecules consisting of an antibody and a cytotoxin; cholesterol-lowering agents; vasodilating agents; agents which interfere with ~~endogeneus~~ endogenous vascoactive mechanisms; survival genes which protect against cell death, such as anti-apoptotic Bcl-2 family factors and Akt kinase; and combinations thereof. Cells can be of human origin (autologous or allogenic) or from an animal source (xenogeneic), genetically engineered if desired to deliver

proteins of interest at the injection site. The delivery mediated is formulated as needed to maintain cell function and viability. Any modifications are routinely made by one skilled in the art.

Please amend paragraph [0051] as indicated below:

[0051] The resin block 71 shown in this illustration may be used to create chemical or ionic forces to draw compounds from the fluid passing through the mixing chamber and also to store those compounds within the catheter 70 after their removal from the fluid. The resin block may also function to prevent the compounds from being reintroduced into the fluid at a later time should the catheter 70 be used in a subsequent or second procedure. The resin block in this embodiment may be permanently fixed in the catheter 70 or it may be replaceable to reuse the catheter 70. Likewise, various other components of this and ~~the~~ other embodiments may also be replaceable as will be evident to one of skill in the art.